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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,565	10/11/2001	Catherine S. Levisage	55322 (71699)	7490

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,565	LEVISAGE ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,37-42,52 and 53* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 14-20, 37-42, 52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, request for continued examination filed under 37 CFR 1.114, amendment and remarks, all filed 7/21/06. Claims 1, 37, 52 and 53 are amended. Claims 1-20, 37-42, 52 and 53 are pending. Claims 12 and 13 remain withdrawn from consideration.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/21/06 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-11, 14-20, 37-42, 52 and 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

Paragraph 44 of the published application defines "microparticle" as "any particle with a mean diameter or particle size in the range of 0.5 μm to 100 μm, with a preference for particles with a mean diameter or particle size in the range of 1 μm to 20 μm which is composed of an approximately homogenous network of the support material. Preferred microparticle geometries are spherical, ellipsoidal and the like. Other polymeric devices included within the term microparticle include but are not limited to nanoparticles, micro or nanocapsules, hydrogels, gels and the like which are capable of encapsulating, or adsorbing or complexing compounds."

The recitation of "particle size of between about 0.5 μm and about 100 μm" was introduced into the claim in the amendment of 4/05/2004. However, the as filed specification does not provide support for a particle size range of "between about 0.5 μm and about 100 μm." What is taught in the as filed specification is as reproduced above, that is, microparticles have particle size in the range of 0.5 μm to 100 μm, with a range of 1 μm to 20 μm preferred. This is true also for the new limitation of "between about 2.0 μm and about 100 μm." The recitation of "about" limits the lower limit of the particle to slightly less than 2.0 μm and the upper limit to be slightly greater than 100 μm and these limitations are not supported by the as filed specification.

The rejection above may be overcome by reciting the particle size range that is supported by the originally filed specification.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-11, 14-20, 37-42, 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bru-Magniez et al. (US 6,211,273).

Bru-Magniez discloses a nanoparticles of polymeric support material network within which therapeutic agents such as taxol and 5-fluorouracil are dispersed (abstract, column 2, lines 35-50, column 5, lines 3-35 and column 6, lines 25-36). The disclosed polymer network meets the polymer structure of the instant claims and the prior art specifically discloses methylidene malonate nanoparticles (column 2, lines 15-17 and Title). The instant method comprises administering the polymeric composition. The prior art administers the composition orally, sublingually, subcutaneously, intramuscularly, intravenously, transdermally, locally, rectally, via the pulmonary route, or nasally; preferred forms of administration notably comprise oral forms, such as tablets, gelatin capsules, powders, granules and oral solutions or suspensions, sublingual and buccal administration forms, as well as subcutaneous, intramuscular intravenous, intranasal or intraocular and rectal administration forms (column 6, lines 43-53). It is inherent that the

administered composition comprising an anticancer drug would inherently provide the desired effect. The nanoparticles of Bru-Magniez have diameter of less that 500 nm and particles having diameter of 100-500 nm are preferred (column 3, line 67 to column 4 line 1). The method of preparing the particles of Bru-Magniez involves preparing a solution of the polymer in a water miscible organic solvent, adding with stirring, the organic phase to an aqueous polymerization medium at a pH between 4.5 and 10, homogenizing the mixture, evaporating the organic solvent in vacuo to recover/collect the nanoparticles (column 4, lines 5-13). In another embodiment, the polymer precipitates in the polymerization medium, the polymer is recovered by filtration and the suspension or filtrate of the nanoparticles is "conditioned and lyophilized" (column 4, lines 14-36). It is noted that the process of recovering precipitates by filtration routinely involves wash cycle(s).

Bru-Magniez discloses the composition and method for preparing the composition. The difference between the prior art and the instant claims is the size of the particles. The prior art discloses particle diameter of less than 500 nm, which is 0.5 μm. The amended claim now has a lower limit of 2.0 μm and applicants' specification and the remarks provide no demonstration that a microparticle having a mean particle diameter of about 2.0 μm provides unusual results. A mean particle diameter of **about 2.0 μm** is nor far removed from particles having diameter of 0.5 μm and absent factual showing, **about 2.0 μm**, which is very close to the particle size of the prior art, is not inventive over the prior art particle diameter of less than 0.5 μm. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the nanoparticle of Bru-Magniez. One having ordinary skill in the art would have been motivated to prepare nanoparticles of methylidene malonate having a diameter of less than 500

nm or 100-500 nm with the expectation that the medicament dispersed within the polymer is delivered to a subject.

Response to Arguments

7. Applicant's arguments filed 7/21/2006 have been fully considered but they are not persuasive.

Examples 6 and 7 do not support particles having sizes of between about 2.0 μm and about 100 μm."

Experiments 5.1 and 5.2 of the Declaration:

The issues on the 1.32 declaration were addressed in the last office action and applicant presents no new data. The response provided in the last office action is valid as it regards to Experiments 5.1 and 5.2.

In Experiment 5.2 of the declaration, an 8-week old mice is used in the experiment. In all the experiments in the declaration, the retention of the polymer in the bladder are described and not the release profile of the drugs; there is also no correlation of the retention with the delivery of drug. The claims are not directed to retention of polymer in the lumen of the bladder, but rather, in instant claim 37, sustained release of drug after administration of the polymer.

Experiment 5.1 of the declaration makes reference to PCT WO 99/55309 while the cited reference is US 6,211,273.

Regarding the particle size, Bru-Magniez discloses particle size of 100 nm (0.1μm) to 500 nm (0.5 μm) while the particle size in claim 1 is about 2.0 μm to about 100 μm. About 2.0

μm does not include 2.0 μm and 0.5 μm is close to about 2.0 μm, the lower particle size limit of applicant's microparticle. The Experiment 4.2 of Dr. Leong's declaration uses 600 nm and while the prior art uses particle of less than 500 nm. The microparticles in Example 4.4 is directed to P(DAPG-EOP), which is not the polymer in the claims. The Examples in the declaration do not describe how much drug is released but the Examples rather discuss retention of the polymer in the bladder lumen. Although, applicants infer that microparticles retained in the bladder are suited for delivery of therapeutics, it is noted that there is no experimental correlation between retention of the polymer and how much drug is delivered or released to the lumen of the bladder. The experiment does not show drug release from particles of less than 0.5 μm and particles of about 1.0 μm. There is no study showing the correlation of retention of the polymer and drug delivery. The method is one of administration and the prior art administers.

P(DAPG-EOP) is not one of the polymers of the examined claims and if one embodiment meets one of the repeat uints of the claim, it is also noted that that particular polymer may be at best one of the possibilities.

Claim 1 does not recite double emulsion technique of preparing the composition of claim 1 and claim 4 is directed to product produced by single emulsification process; thus the Experiment 4.1 discussing double emulsion process is not commensurate with the claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech. Center